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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,002	01/26/2004	Keenan Martin Bora	U 015009-1	6762

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/765,002	BORA ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

DETAILED ACTION

1. Claims 1-22 are pending in the application.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 8-31, 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight different factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The instant compounds are shown to be BCAT inhibitors in vitro as shown by experimental data in table 1 on page 144. Based on this data, the instant compounds

will have utility in treating but not preventing only those disease conditions where BCAT inhibitors are well known in the prior art to have therapeutic utility. There is no teaching either in the specification or prior art references provided showing well known utility of BCAT inhibitors. There are no working examples present showing efficacy of instant compounds in known animal models of any disease condition mentioned in instant claims 8, 21 and 22. The instant compounds of formula I encompasses several hundreds of thousands of compounds based on the values of variables R1- R5 and Ar and therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to demonstrate the efficacy of instant compounds in known animal models of all the disease conditions listed in instant claims 8, 21 and 22 and hence their utility for treating these disease conditions.

It is well known in the art that there are multiple mechanisms involved in the etiology of any known disease condition and therefore, correcting only one of these mechanisms will not prevent (completely cure) that specific disease condition.

Claims 1-22 are also rejected for lack of enablement in regard to the terms, ester, prodrug or amide in claim1. There is no teaching regarding specific prodrugs, esters or amides in the specification. There is not even a single example present of ant ester, prodrug or amide in the specification. There is lot of unpredictability regarding effectiveness of different types of prodrugs following their in vivo administration since their effectiveness depends upon release of parent compound to its target and is influenced by various factors such as absorption, destruction by esterases etc. in the

gut. In view of large number of compounds encompassed by the instant compounds of formula I, it would require undue experimentation to select and prepare specific prodrugs, esters or amides which will be effective following in vivo administration.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 6, 8-19, 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the terms ---ester, prodrug, or amide ---- are indefinite since specific esters, prodrugs or amides are not defined.

In claims 8-13, 21 and 22, the term—preventing--- is indefinite since the degree of prevention (20%, 40%, 60%, 80% or 100%) is not defined and furthermore, how this prevention is being assessed in vivo?

In claims 14-19, the term ---therapeutically effective ----- is indefinite since it is not clear which disease condition is being treated. The claim is directed to inhibiting enzyme activity only and not treating any disease condition.

Claims 6, 13 and 19 recite the limitation "Naphthalene for the value of variable Ar (see compounds in lines 15-29 on page 157, lines 1-16 on page 168, lines 9-24 on page 178 and last compound on pages 170 and 181" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 21 provides for the use of compound of formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process

applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 21 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1,2,5-7, 14-16 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Koruncev (Acta Pharm. Jugos., cited on applicants form 1449). Koruncev discloses antibacterial and antiviral effects in a series of hydrazides and hydrazones derived from quinoline-2-carboxylic acid. The compounds 5-7 (see table II on page 243) disclosed by koruncev anticipate the instant claims when Ar represents quinoline in the instant compounds of formula I.

9. Claims 1, 3, 5-7, 14, 16 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Nour El-Din (U.A.R. J. Pharm. Sci., cited on applicants form 1449).

Nour El-Din discloses synthesis of bergapten and some of its derivatives having molluscicidal activity. The compound V (see page 46) and its preparation from compound IV disclosed by Nour El-Din anticipates the instant claims when Ar represents benzofuran in the instant compounds of formula I.

10. Claims 1, 2, 5, 6 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhat (J. Chem. Soc., cited on applicants form 1449).

Bhat discloses synthesis of indole-2-carbaldehydes, 2-(2-aminoethyl)-and 2-(2-aminopropyl)-indoles. The compound III (see page 179) and its preparation from compound II disclosed by Bhat anticipates the instant claims when Ar represents an indole in the instant compounds of formula I.

11. Claims 1, 2, 4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Carter (J. Chem. Soc. Abstracts).

Carter discloses Formyl derivatives of carbazole and 1, 2, 3, 4-tetrahydrocarbazole. The compounds disclosed on page 2212 (see third paragraph) by carter anticipates the instant claims when Ar represents tricyclic heteroaryl ring in the instant compounds of formula I.

12. Claims 1, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Hagen (U.S. Patent no. 4,797,148).

Hagen discloses quinoline derivatives for controlling undesirable plant growth. The exemplified compound 11 (see col. 8) disclosed by Hagen anticipates the instant claims when Ar represents quinoline in the instant compounds of formula I.

13. Claims 1, 3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Loccufier (U.S. Patent no. 5,558,974).

Loccufier discloses photographic material containing a new type of hydrazide. The exemplified compounds 111.6, 111.15 and 111.10 (see columns 22-25) disclosed by Loccufier anticipates the instant claims when Ar represents isoquinoline, benzthiazole or benzimidazole in the instant compounds of formula I.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
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Art Unit 1625